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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Artcle 36 and Rule 70)

Applicant's or agent's file reference NO-20994-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. **PCT/KR2003/001449**	International filing date *(day/month/year)* **22 JULY 2003 (22.07.2003)**	Priority date *(day/month/year)* 22 JULY 2002 (22.07.2002)

International Patent Classification (IPC) or national classification and IPC

IPC7 A61K 47/02

Applicant

NANOHYBRID CO., LTD. et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demamd	Date of completion of this report
19 FEBRUARY 2004 (19.02.2004)	08 NOVEMBER 2004 (08.11.2004)

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International aplication No.
PCT/KR2003/001449

I. Basis of the report

1. With regard to the elements of the international application:*

- [X] the international application as originally filed
- [ ] the description:
  pages _____, as originally filed
  pages _____, filed with the demand
  pages _____, filed with the letter of _____
- [ ] the claims:
  pages _____, as originally filed
  pages _____, as amended (together with any statment) under Article 19
  pages _____, filed with the demand
  pages _____, filed with the letter of _____
- [ ] the drawings:
  pages _____, as originally filed
  pages _____, filed with the demand
  pages _____, filed with the letter of _____
- [ ] the sequence listing part of the description:
  pages _____, as originally filed
  pages _____, filed with the demand
  pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language English which is

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [X] the language of publication of the international application(under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/ or 55.3).

3. With regard to any **nucleotide** and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- [ ] contained inthe international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disc losure in the international applicationas as filed has been furinshed.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages _____
   - [ ] the claims, Nos. _____
   - [ ] the drawings, sheet _____

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box(Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed." and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1 - 15	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1 - 15	NO
Industrial applicability (IA)	Claims	1 - 15	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents have been considered for the purpose of this report; the numbering will be adhered to in the rest of the procedure:

D1 : JP 13278810 A (10 October 2001)
D2 : Biomaterials; Vol. 23, pp.1981-1987 (May 2002)

1. Novelty

Claims 1 - 15 relate to a hybrid of a drug with layered silicate having good solubility and bioavailability, and the production process thereof.

D1 and D2 disclose the method of solubilization for a poorly water-soluble drug by intercalating a drug into layered silicate. However, the present invention is different from D1 and D2 in the kind of the drug to be intercalated. Indomethacin and 5-FU are described in the prior arts, whereas the drug selected from a group consisting of itraconazole, cyclosporine and carvedilol, is intercalated between the layers or adsorbed onto the surface of silicate in the present invention.

Therefore, the subject matter of claims 1 - 15 is novel over D1 and D2 [PCT Article 33(2)].

2. Inventive Step

D1 discloses a pharmaceutical composition comprising poorly-soluble drug and layered silicate, which increases solubility of the drug. D1 also discloses the preparation method characterized by mixing a drug dissolved in organic solvent with water-dispersed layered silicate, followed by removing the solvent. The technical feature of D1 is the same as claims 1- 15 of the present invention.

(Continued on Supplemental Sheet.)

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VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The meaning of "hybrid" in claims 1 - 15 is not clear, and expresssion "about" for the pH and percent amount in claims 8-12 are vague.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of:

Box V.

Even though the intercalated drug of present invention is different from D1, a various kind of drug such as antibiotics and anti-hypertensive agent are described in D1. In addition, D2 describes that 5-FU has been intercalated into montmorillonite by surface adsorption and isomorphous substitution, and intercalating a cationic compound into montmorillonite comes within a customary practice. The drug of the present invention, itraconazole, cyclosporine, and carvedilol, becomes cationic when the amine group is converted to ammonium. As a consequence, it might be obvious for a person skilled in the art that a hybrid of the present invention shows enhancement in solubility and bioavailability.

Accordingly, the inventive step could not be acknowledged for claims 1-15 [PCT Article 33(3)].

3. Industrial Applicability

Claims 1-15 are industrially applicable under PCT Article 33(4).